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No. 86-1633

In the Supreme Court of the United States

OCTOBER TERM, 1986

NORWICH EATON PHARMACEUTICALS, INC.,
PETITIONER

v.

OTIS R. BOWEN, SECRETARY OF HEALTH
AND HUMAN SERVICES, ET AL.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE SIXTH CIRCUIT

BRIEF FOR THE RESPONDENTS IN OPPOSITION

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QUESTION PRESENTED

Whether the Food and Drug Administration acted arbitrarily or capriciously when it decided that the date on which the agency had approved petitioner's new drug application for the drug Buprenex was December 29, 1981, and, on the basis of that factual finding, concluded that petitioner was not entitled to benefit from exclusive marketing provisions that are reserved by statute for drugs approved after 1981.

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OPINIONS BELOW

The opinion of the court of appeals (Pet. App. 1a-14a) is reported at 808 F.2d 486. The decision of the district court (Pet. App. 15a-21a) is reported at 645 F. Supp. 321. The decision of the Food and Drug Administration (Pet. App. 22a-30a) is unreported.

JURISDICTION

The judgment of the court of appeals was entered on January 9, 1987. The petition for a writ of certiorari was filed on April 9, 1987. The jurisdiction of this Court is invoked under 28 U.S.C. 1254(1).

STATEMENT

1. a. The Federal Food, Drug, and Cosmetic Act of 1938 established a system of premarketing clearance for drugs. *United States* v. *Generix Drug Corp.*, 460 U.S. 453, 458 (1983); *Weinberger* v. *Hynson, Westcott & Dunning*, 412 U.S. 609, 612 (1973). Section 505(a) of the Act, 21 U.S.C. (Supp. III) 355(a) prohibits any person from introducing into interstate commerce any "new drug" for which the Food and Drug Administration (FDA) has not approved a "new drug application" (NDA). Section 505(b) of the Act, 21 U.S.C. (Supp. III) 355(b), requires that an NDA contain: (1) reports of tests that show the drug is safe and effective for its intended use; (2) the drug's components and composition; (3) a description of the methods and controls used in manufacturing, processing and packing; (4) samples of the drug if the Secretary so requires; and (5) specimens of proposed labeling for the drug. Section 505(c) of the Act, 21 U.S.C. (Supp. III) 355(c), requires that the Secretary must approve or disapprove an NDA within 180 days of its submission, subject to extension by agreement of the parties. See *Weinberger* v. *Hynson, Westcott & Dunning*, 412 U.S. at 613.[1]

Under a regulation promulgated under the Act when the agency approves an NDA it is required to provide written notice to the applicant "that the application is approved and the application shall be approved on the date of the notification." 21

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[1] The authority to approve new drugs, granted by statute to the Secretary of Health and Human Services, has been delegated to the Commissioner of Food and Drugs (21 C.F.R. 5.1(a)(1) (1981); see 46 Fed. Reg. 26052 (1981); 21 C.F.R. 5.10(a)(1)), and to certain other specified officials of the FDA (21 C.F.R. 5.80(a) (1981); 21 C.F.R. 5.80 (1987)).

C.F.R. 314.105 (1981). That regulation, as subsequently amended, today provides that "[t]he date of the agency's approval letter is the date of approval of the application." See 21 C.F.R. 314.105(a) (1987). The prior version of this regulation had been in force since 1963. 21 C.F.R. 130.10 (1963); 28 Fed. Reg. 6377 (1963).

b. The Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585, amended the Act to provide a streamlined procedure for the approval of so-called generic drugs, which are copies of original, or "pioneer," drugs already approved by the FDA. See H.R. Rep. 98-857, 98th Cong., 2d Sess. 14 (1984); see also *United States* v. *Generix Drug Corp.*, 460 U.S. at 454-455; *Inwood Laboratories, Inc.* v. *Ives Laboratories, Inc.*, 456 U.S. 844, 846-848 & nn. 4, 5 (1982). The streamlined approval format, known as an Abbreviated New Drug Application (ANDA), is designed to enhance the competition between generic drugs and pioneer products by reducing the costs and time of obtaining regulatory approval to market generic drugs.

As part of the legislative compromise underlying the 1984 amendments, Congress provided that pioneer drugs approved by the FDA after January 1, 1982, would be entitled to certain periods of marketing exclusivity independent of that provided by patent: a pioneer drug containing a new chemical entity approved between January 1, 1982, and September 24, 1984, is entitled to ten years of marketing exclusivity (21 U.S.C. (Supp. III) 355(j)(4)(D)(i) and 355(c)(3)(D)(i)); a pioneer drug containing a new chemical entity and approved after September 24, 1984, the effective date of the 1984 amendments, is entitled to five years of exclusivity (21 U.S.C. (Supp. III) 355(j)(4)(D)(ii) and 355(c)(3)(D)(ii)).

2. a. Petitioner is a pharmaceutical company that filed an NDA on October 31, 1979, seeking approval of its pioneer analgesic drug, Buprenex, which contains the active ingredient buprenorphine hydrochloride. After an examination of the product's safety and effectiveness, and of the product's proposed labeling, the FDA, on October 14, 1981, notified petitioner that changes in the product's proposed labeling would be required before the product could be approved (Pet. App. 2a, 5a, 27a-28a). Subsequently, in a December 22, 1981, telephone conversation, petitioner agreed to the labeling changes (*id.* at 24a).

On December 29, 1981, FDA's Associate Director for New Drug Evaluation wrote to petitioner, stating that the Buprenex NDA had been approved. Because buprenorphine hydrochloride, the active ingredient in Buprenex, is derived from the opiate thebaine, it is a narcotic drug subject to the Controlled Substances Act, 21 U.S.C. (& Supp. III) 801 *et seq.*, which is administered by the Drug Enforcement Agency (DEA). When the FDA approved the new drug application for Buprenex in December 1981, buprenorphine hydrochloride was classified by the Controlled Substances Act as a Schedule II drug, but proceedings were in progress to place the drug onto a less restrictive schedule. In approving Buprenex, the FDA stated that the drug could presently be marketed as a Schedule II drug despite any on-going rescheduling proceedings before DEA. The December 29, 1981, approval letter stated (Pet. App. 3a):

> We have completed the review of this application and have concluded that the drug is safe and effective for use as recommended in the labeling. * * * Accordingly, the application is approved.

> As you know, the Division is preparing documents to affect lesser controls for buprenorphine. This, however, in no way impairs your approval to market buprenorphine in its current controlled substances schedule.

In a letter to the FDA dated February 3, 1982, petitioner's president unequivocally acknowledged that the agency's "Office of New Drug Evaluation approved Norwich Eaton's New Drug Application for [Buprenex] on December 29, 1981" (Pet. App. 25a; see *id.* at 3a; C.A. App. 383). Petitioner thereafter provided FDA with the quarterly, semi-annual and annual reports required for approved new drugs. See Pet. 10; 21 C.F.R. 310.300(b)(4)(i) (1981).

On February 28, 1985, the DEA concluded its proceedings concerning the rescheduling of buprenorphine hydrochloride; it placed that substance on Schedule V of the Controlled Substances Act, the least restrictive category for substances subject to control under that statute. See 50 Fed. Reg. 8104 (1985).

b. On August 19, 1985, almost four years after the FDA had approved the NDA for Buprenex, and several months after the effective date of the 1984 amendments, petitioner filed a "citizen's petition" with the FDA under 21 C.F.R. 10.30, seeking a declaration that Buprenex qualified for non-patent marketing exclusivity under the 1984 amendments because the NDA for the drug Buprenex had been approved after January 1, 1982. Petitioner stated that although the agency issued a letter approving the Buprenex NDA on December 29, 1981, "there did not exist at that time FDA approved labeling under which the product could have been marketed" (C.A. App. 26). Petitioner claimed that as of December 29, 1981, Buprenex had not been assigned a schedule un-

der the Controlled Substances Act that was acceptable to petitioner. In addition, petitioner contended that final labeling was not approved until June 28, 1985, after buprenorphine hydrochloride had been rescheduled by DEA, and that this latter date was therefore the date on which the NDA filed in 1979 was actually approved. Under this theory, petitioner claimed that it was entitled to a five-year period of marketing exclusivity under the 1984 amendments. In the alternative, petitioner argued that the approval of its product occurred not on the date the FDA approval letter was issued (December 29, 1981), but on the date the letter was received (January 8, 1982). Under this alternative theory, petitioner claimed that it was entitled to a ten-year period of marketing exclusivity.

c. The FDA denied the petition (Pet. App. 22a-30a). In its opinion, the agency concluded that the letter of December 29, 1981, had unequivocally approved the NDA for Buprenex; that the statutory term "date of approval" refers to the date on which "the agency exercises its authority * * * to approve a new drug application" (see 21 C.F.R. 314.105 (1981)), not to the date an approval letter is received; and that approval is not contingent on a meeting of the minds between the FDA and the applicant on the terms of the approval. The agency explained that an NDA is approved when the statutory requirements for approval are met. Pet. App. 24a-29a.

In response to petitioner's assertion that Buprenex could not have been approved on December 29, 1981, because the drug was not then "scheduled" by DEA, the agency stated (Pet. App. 28a) that classification within a particular schedule under the Controlled Substances Act is not a statutory prerequisite to ap-

proval of a drug, and that, in any event, the drug's active ingredient, buprenorphine hydrochloride, was a derivative of the drug thebaine and therefore was statutorily classified as a Schedule II drug at the time the NDA for Buprenex was approved (see 21 U.S.C. (1976 ed.) 812(c)). Accordingly, the agency explained, Buprenex could have been marketed as a Schedule II drug on the date its NDA was approved.

The agency also rejected petitioner's contention that the Buprenex NDA was not approved until June 28, 1985, the date on which the FDA approved certain labeling for the drug. First, the agency noted, the June 28, 1985 letter stated that it constituted approval of an amended *supplemental* application—not approval of the original NDA which had been approved in 1981 (Pet. App. 26a). The FDA also observed that the letter of June 28, 1985, upon which petitioner relied, was signed by an agency official who, while having authority to approve supplemental applications, lacked authority to approve NDAs (*ibid.*). As the agency explained, even if petitioner were correct in contending that the Buprenex NDA had not been approved prior to June 28, 1985, the letter of that date could not constitute such approval and, in that event, petitioner had no authority to market its drug at all and no basis to claim exclusivity (*id.* at 26a-27a).

3. Petitioner challenged the agency's decision by commencing this lawsuit; it sought a declaration that the Buprenex NDA had been approved on June 28, 1985, and that petitioner was therefore entitled to a five-year period of marketing exclusivity under the 1984 amendments. The district court granted the relief petitioner requested. It held (Pet. App. 19a) that the agency's letter of December 29, 1981, was

only a "conditional approval." In the court's view, an approval could not be other than conditional until the product had final printed labeling containing a designation under the Controlled Substances Act that was satisfactory to the applicant (*ibid.*). The court concluded that final labeling was not approved until June 28, 1985, after Buprenex's classification under the Controlled Substances Act was changed from Schedule II to Schedule V. On that premise, the court held that Buprenex was not approved until June 28, 1985, and therefore that petitioner was entitled to a five-year period of marketing exclusivity under 21 U.S.C. (Supp. III) 355(j)(4)(D)(ii).

4. The court of appeals unanimously reversed. As a threshold matter, the court determined (Pet. App. 6a) that the only issue before it, and the only issue properly before the district court, was whether the FDA had acted arbitrarily or capriciously or had abused its discretion in deciding that Buprenex had been approved on December 29, 1981.

Turning to the merits, the court held that the FDA's interpretation of when a drug is approved, viz., on the date which appears on the approval letter, "is reasonable and enables [the agency] to fulfill its statutory mandate" (Pet. App. 9a). The court found nothing in the statute or regulations that would prevent the FDA from approving Buprenex on the basis of proposed labeling, since the Federal Food, Drug, and Cosmetic Act requires the applicant only to submit specimens of the labeling " 'proposed to be used for such drug' " (*id.* at 8a (quoting 21 U.S.C. (1976 ed.) 355(b)(6) and 21 U.S.C. (Supp. III) 355(b)(1)((F)). Thus, in the court's view, the statute "cannot be read to require submission of final printed labeling before approval" (Pet. App. 8a).

ARGUMENT

The decision of the court of appeals is correct and does not conflict with any decision of this Court or of any other court of appeals. The decision below is fact-specific and hence does not present a question of importance other than to the parties. Further review is therefore not warranted.

1. As the court of appeals recognized, the sole question at issue in this case is whether the FDA's denial of petitioner's citizen's petition was arbitrary or capricious. The agency's determination of the particular date on which petitioner's NDA for Buprenex was approved, a conclusion in which the court of appeals concurred, does not merit review on certiorari. Cf. *Mobil Oil Corp.* v. *FPC*, 417 U.S. 283, 310 (1974); *Universal Camera Corp.* v. *NLRB*, 340 U.S. 474, 491 (1951).

In any event, the FDA's determination that the date on which petitioner's new drug application had been approved mandated a denial of petitioner's request for exclusivity under the 1984 amendments was not arbitrary or capricious. In construing the term "approved" in the Federal Food, Drug, and Cosmetic Act, the FDA concluded that a new drug application is considered approved on the date stamped on the approval letter. See 21 C.F.R. 314.105 (1981). In this case, the FDA approved petitioner's new drug application in a letter dated December 29, 1981. Given that date of approval, the FDA was clearly correct in determining that petitioner's drug Buprenex did not qualify for the exclusive marketing benefits that the Act reserves for drugs approved on or after January 1, 1982.

The FDA's determination that the new drug application for Buprenex was approved on December

29, 1981, is thus supported by the agency's regulation governing when an NDA is approved and by the express language of the approval letter, which states unequivocally that "the application is approved" (Pet. App. 3a). Indeed, that determination is further corroborated by the acknowledgment by petitioner's president, on February 3, 1982, that Buprenex had been approved by the FDA on December 29, 1981, and by petitioner's subsequent filing of the quarterly, semi-annual and annual reports required by 21 C.F.R. 310.300(b)(4)(i) (1981) for *approved* drugs.

2. a. Petitioner contends (Pet. 18-22) that an NDA cannot be approved unless the agency has approved final printed labeling, as opposed to draft labeling, and that final labeling cannot be approved unless and until the drug has been assigned to a schedule under the Controlled Substances Act which is acceptable to the pharmaceutical manufacturer. Petitioner therefore claims that the FDA approval of Buprenex on December 29, 1981, was merely conditional, and hence was an insufficient basis on which to conclude that petitioner is not eligible to benefit from the exclusive marketing provisions of the 1984 amendments.

Petitioner has incorrectly perceived the applicable law. The approval of a new drug under the Federal Food, Drug, and Cosmetic Act is not dependent upon scheduling under the Controlled Substances Act or upon the approval of final printed labeling. The FDA must timely approve a new drug application if none of the grounds for disapproval set forth in 21 U.S.C. (Supp. III) 355(d) is present. See 21 U.S.C. (Supp. III) 355(c)(1). Thus, if a product is found to be safe and effective when taken as the

proposed labeling directs, the drug must be approved (see 21 U.S.C. (Supp. III) 355(d)(1) and (d)(6)).[2] Drug scheduling under the Controlled Substances Act is irrelevant to FDA's approval process and is performed under the wholly separate authority of the DEA. See 21 U.S.C. (& Supp. III) 801 *et seq.* Had Buprenex been unscheduled by the DEA, it would have been approved as an unscheduled drug by the FDA. Here, however, it was placed in Schedule II by an Act of Congress and upon approval of the new drug application by the FDA, Buprenex could have been marketed as a Schedule II drug.

There are significant flaws in petitioner's suggestion that final approval of the drug by the FDA had to await further rescheduling action by the DEA. At the time the FDA approval letter was issued, proceedings were already underway to consider placing buprenorphine hydrochloride, Buprenex's active ingredient, into a less restrictive schedule that was more acceptable to petitioner. The drug approval system created would be unworkable if the FDA could not approve a new drug application that met all statutory criteria, simply because there was a possibility that the DEA might change the schedule of

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[2] The district court, in ruling that an NDA cannot be approved until the final printed labeling is approved, ignored the lack of such a requirement in the statute. Instead, the court cited (Pet. App. 19a) 21 C.F.R. 314.1(c)(4)(e) (1981), a regulation which provides that an NDA "will not ordinarily be approved prior to the submission of the final printed label and labeling of the drug."

As the court of appeals correctly held, the use of the word "ordinarily" in the regulation assumes "that on some occasions the FDA will approve an application based on draft labeling" (Pet. App. 8a), which is exactly what occurred in this case.

the drug in question. Similar practical difficulties would exist if, prior to approving a new drug application, the FDA were required to achieve a "meeting of the minds" with the applicant over suitable scheduling—a subject over which the DEA presides. The statute does not require that the fate of a new drug application be determined by the DEA or left entirely to the predilection of the applicant.

b. Petitioner also claims (Pet. 22-29) the court of appeals erred by deferring to the FDA's interpretation of the statute it administers and the regulations promulgated thereunder. It is petitioner's submission that the FDA has no expertise in questions of non-patent exclusivity, that the agency did not engage in adequate factfinding procedures, and that the agency decision may have been biased.[3]

The short answer to these contentions is that this case involves the FDA's construction of a term in its operating statute and, as this Court has repeatedly held, substantial deference to the agency interpretation is required. *Young* v. *Community Nutrition Institute*, No. 85-664 (June 17, 1986), slip op. 5-6; *Chevron U.S.A. Inc.* v. *Natural Resources Defense Council, Inc.*, 467 U.S. 837 (1984); *United States* v. *Rutherford*, 442 U.S. 544, 553 (1979). The deference to which the agency is entitled is not diminished by petitioner's contention that the agency "failed" to engraft additional procedures onto the approval scheme Congress established in the Federal Food, Drug, and Cosmetic Act. The agency carried

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[3] Petitioner's charge of potential bias has no support in the record and petitioner has been unable to point to any such bias in this case. Indeed, the petition acknowledges (Pet. 28) that "in the present case, FDA may have no particular bias against Norwich * * *."

out the tasks Congress directed by evaluating the Buprenex NDA under the statutory criteria, which include safety, effectiveness, and proposed labeling. The agency was not required to do more and its rational determination was correctly upheld by the court of appeals. Cf. *Vermont Yankee Nuclear Power Corp.* v. *Natural Resources Defense Council, Inc.*, 435 U.S. 519 (1978).

CONCLUSION

The petition for a writ of certiorari should be denied.

Respectfully submitted.

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